The Transmission of Leprosy by Mosquitoes and its Prophylaxis

by

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This paper was presented to the Section of Tropical Medicine, of the 7th Cruise-Congress of the Pan American Medical Association, whose invitation to be present at the meeting held at Havana, in January 1938, I was unable to accept.

The subject was chosen as leprosy is one the most important medical problems as yet unsolved and I do not believe its eradication to be possible until methods of prophylaxis are subjected to an entirely different approach.

Following the paper a series of experiments are suggested for the demonstration of the possibility of the transmission of pathogenous germs belonging to the same group as that of leprosy by mosquitoes. They and the methods to be used were first suggested by me at a meeting of the Brazilian Academy of Science, when I received its Einstein Prize (1935).

The idea of the transmission of leprosy by blood-sucking insects is not new. It was stated by various observers already at a time when our knowledge of their importance was still quite rudimentary. The supposition then prevalent was that the insects functioned somewhat like vaccine-lancets, first inserting their mouth-parts in the diseased tissue of a leper, then in the healthy skin of another person, thus infecting him or her. This simple point of view did not, however, agree sufficiently with the mechanism of propagation observed in other important mosquito-transmitted diseases, to make it generally acceptable.

Let us recall some of these, for instance the first observations on human blood-parasites developing in mosquitoes. These were made as early as 1877 on Filaria bancrofti by Manson. The process of transmission, however, was only explained in 1900 by Bancroft and Low. Before this (1888-1889), Smith and Kilbourne had already demonstrated the transmission of Texas fever by ticks, and Ross and Grassi that of malaria by mosquitoes (1898). Finally the transmission of yellow-fever by a house-mosquito was experimentally established in Cuba by Reed and Caroll and confirmed in the same year in S. Paulo (Brazil),
by some volunteers, among whom Dr. E. Ribas and the author of this paper.

It was only after these investigations had taken place and were confirmed by the results of anti-mosquito prophylaxis that the importance of blood-sucking animals in the spreading of infectious diseases was understood.

It also became evident that this is no simple process of puncture and inoculation but that the change of hosts is essential to the development of the blood-parasite, and also that a lapse of time is necessary before the intermediate blood-sucking host becomes infectious. This explains why Finlay’s experiments could not furnish convincing proof of the transmission of yellow-fever by mosquitoes. He did not know that a period of from ten to eleven days had to pass between the bite that infects the mosquito and the bite that transmits the disease to a new victim.

At the end of the last century bubonic plague re-appeared in many places and led to the discovery and study of its causal germ which, in this case, is a true bacterium; but the fact that it is usually transmitted by fleas biting rats and men followed only after several years of patient study.

On the whole, one may say that the rôle of blood-sucking insects and arachnids in the spreading of diseases was found out at the end of the last century but that it was only in the beginning of the present one that the investigation of all these blood-sucking, temporary or permanent, parasites was carefully undertaken. The results were most interesting; not only was the number of blood-sucking species discovered and classified much greater than could originally have been expected, but also the diseases transmitted by them alone turned out to be much more numerous than was at first presumed. An enquiry recently undertaken by myself and an assistant, Dr. G. M. de Oliveira Castro, from the Veterinary School in this city, on the diseases of man, domestic and common wild animals transmitted by blood-suckers, published in Portuguese (1), showed the following results: both parasites and transmitters belong to many different classes; the latter range from blood-sucking mammals (bats) and worms (leeches) to arachnids (ticks and mites) and insects (very numerous diptera and less numerous, but quite as important, hemiptera, fleas and lice). Besides many worms (principally Filariae) and Protozoa they transmit some Sehizomyctae and diverse virus-diseases. Altogether the number of parasitical and infectious processes transmitted exclusively, or mainly, by blood-suckers can be estimated between 50 and 100, and their number is continually increasing.

Nowadays it may be said that a blood-sucking animal is the normal
way for parasites living in the circulatory system to pass from one individual to another. Every new disease has to be investigated along these lines.

Personally, I have studied the blood-sucking animals of South-America for nearly half a century, and place the number of species at several hundred, of which about 300 Diptera alone. As regards human diseases the common mosquitos (Culex, Stegomyia, Anopheles) and Phlebotomus species are the most pernicious, but for animals the ticks and the house-flies (Tabanidae) are especially important. The Tabanidae are very numerous and their rôle has not been sufficiently investigated as yet.

Zoologists studying insects and arachnids described many blood-sucking species in different countries, as early as the beginning of the nineteenth century. The mosquitos, being more fragile than the Tabanids, were not so easy to preserve and this led to a great deal of synonymy.

In 1926 there appeared an extensive report on the transmission of dengue by Stegomyia aegypti. This mosquito, which transmits yellow-fever, was found also to cause epidemics of dengue, a disease which has practically no mortality; it was used for very numerous experiments on volunteers in Manila, and the results entirely confirmed anterior statements (2).

When the study of the transmission of malaria and yellow-fever was already practically complete and mosquitos had been extensively studied, Blanchard gave a good summary of the arguments in favour of the transmission of leprosy by them (3). In consequence of these and similar considerations, some leprologists began to examine mosquitos which had bitten leprous patients, and in some cases found acid-fast rods in them. Others experimented with the bites of such mosquitos without obtaining convincing results. But it is very easy to see that all those experiments were not well conducted, as I have explained in former publications. Among other reasons, no allowance was made for the time of incubation inside the mosquito.

It is obviously not advisable to experiment on man. There have, however, been observed several rather similar parasitical processes in small birds, rats and water-buffaloes (Bos bubalus or carabao), with which experiments could easily be performed, always allowing for a protracted incubation. In these lepra-like infections there are to be found organisms resembling in form, number, and staining reaction, the organism now generally, but erroneously called Mycobacterium leprae. Already in 1886 I proposed the generic name of Coccothrix for the germs of Leprosy and Tuberculosis, after a careful...
study of their forms and staining properties, and this name has undoubted priority-rights (4).

The transmission of leprosy by mosquitoes always appealed to me, principally after I observed how common the two house-mosquitoes (*Stegomyia aegypti* and *Culex quinquefasciatus*) were in the Hawaiian Island (1889-1891), while other blood-sucking diptera were entirely absent. At that time the knowledge of the rôle of mosquitoes as transmitters of diseases was not sufficiently advanced to permit of more than a supposition. In the last 25 years, however, I have, on various occasions, insisted on the probability that domestic mosquitoes are the only transmitters of this disease and have given a number of convincing arguments, so that at least in South America no leprologist need be ignorant of them.

In 1936 I summarily reviewed the whole litterature and published an extensive paper on the transmission of leprosy, which appeared in German, and, in a somewhat abridged form, in English and Portuguese (5). The contents were transcribed in French and Italian medical papers and reviews, and copies were distributed among leprologists, so that the idea was sufficiently made known. As on former occasions, I received several supporting opinions and this time found no opposers, so that I may assume that I have sufficiently proved what I have advanced. The main arguments in favour of the transmission of leprosy by mosquitoes will be found at length in that publication. In summary they are as follows:

I — Hundreds of imported cases interned in hospitals in Paris, London and Vienna do not produce new infections either among the patients, medical and nursing staff or other persons. Patients infected abroad do not give rise to new foci in countries free from leprosy.

These facts can only be explained by the absence of a transmitter which serves as a link.

II — Many people, infected with leprosy, among them quite a number of patients of mine, have never had direct contact with other lepers. They generally show the first localisations on the parts of the body normally exposed to mosquito bites, such as the face and hands.

Transmitters other than blood-sucking Diptera have to be excluded, because they are just as common in lepra-free countries as in those where leprosy still exists, whether it be increasing or just stationary.

1 Including from Drs. Jesus M. Gomes, from Guindolim, Goa, Portuguese India and Pesckowsky, Director of the Clinical and Experimental Leprosy Station in Krasnodar in charge of the epidemiological work in the territory from Azor to the Black Sea. The latter says his patients come from a zone infested by blood-sucking diptera and that many of them had never seen other lepers,
III — Domestic mosquitoes abound in all countries where leprosy is endemic.

In Hawaii, where I worked on leprosy myself, the introduction of mosquitoes was followed by the rapid dissemination of leprosy, and the archipelago became one of its most intense foci. The extensive rice and taro cultures undoubtedly provided an excellent habitat for the mosquitoes introduced. The same phenomenon probably occurred in all the other Polynesian Islands where mosquitoes and leprosy were formerly unknown.

IV — Direct experiments to transmit leprosy by inoculation of human beings and animals have almost constantly given negative results.

This shows that such is not the normal way of transmission.

V — The Coccotrichia of leprosy and tuberculosis are not always acid-fast. They show granulations either free or strung on filaments. These granulations can pass through filters.

It is quite possible that these granulations will prove to be the really infectious form.

Yet leprologists still fail to realize the urgency of prophylactic measures against mosquitoes, though they promise much better results than the treatment of already confirmed cases.

In most countries where leprosy is progressing, or at least not diminishing, sanitary legislation and its enforcement quietly ignore such prophylaxis. It must not be forgotten that mosquitoes are not limited to warm countries but are quite prevalent in all places where leprosy is endemic. The name "mosquito" is not used everywhere but, of course, it should be considered to include all blood-sucking Culicidae often known by other names, such as gnats, cousins (fr.) etc. which are especially dangerous when they occur inside houses or in the neighbourhood of human habitations.

The study of Culicidae is now so far advanced that most of the important forms have been described and sanitary authorities cannot afford to neglect them as they are an essential factor in Public Hygiene. Where yellow fever, dengue and malaria are prevalent, mosquito-prophylaxis is already understood to be of the utmost importance and practised with great energy.

The same should apply to leprosy. The technique has been extensively elaborated and discussed and need not be explained again.

In conclusion, I limit myself to proposing some absolutely indispensable rules, which ought to be observed even by those who do not admit that the mosquito is the only transmitter of leprosy:
I — In every leper-hospital or settlement there ought to be at least one person appointed to maintain a strict and continuous anti-mosquito prophylaxis. In larger hospitals or settlements, this person ought to be a properly trained entomologist or medical officer. Any mosquito found on the premises must be accurately determined and registered. The result of such observations should be included in every periodical report of the establishment.

II — When patients are admitted they must be questioned on the mosquito conditions in the place where infection probably took place and their indications must be controlled by further reliable investigations. For statistical purposes the localisation of the first cutaneous lesions must be carefully made note of in all cases of leprosy.

III — Feverish patients and those whose disease is rapidly progressing ought to be isolated from the others in special screened wards.

IV — Leper hospitals and settlements should be located in places not likely to be invaded by swamp or wood-mosquitos, though the domestic ones seem by far the most important. The rooms must not offer hiding places or badly lighted corners. Dark wall papers should not be used. Windows and doors must be screened with wire frames which cannot be left open. No human habitations must be allowed in the vicinity unless they are included in the prophylactic arrangements.

V — Before the screens are put up all mosquitos found on the premises must be collected and examined. The whole premises must be daily examined for breeding places of mosquitos; the larvae of the mosquitos bred there must be determined.

VI — It is absolutely essential that in all regions where there is leprosy a careful study of all existing blood sucking diptera and their habits should be officially undertaken in order to direct prophylaxis.

VII — Prophylaxis against mosquitos is justifiable and useful in itself.

VIII — The isolation of lepers as carried out until now, without mosquito-prophylaxis, has not led to the eradication of leprosy, though practised in some places for thousand of years as in China, for instance. A hundred thousand new cases arise each year in the world. To segregate human beings without ensuring the safety of others is not only illogical but unjust.

IX — When old methods prove insufficient, new methods must be tried.
EXPERIMENTS INTENDED TO PROVE THE POSSIBILITY OF TRANSMISSION OF LEPROSY BY MOSQUITOS

I propose that experiments be carried out by infecting mosquitoes chosen among species that bite readily. The common nocturnal mosquito, *Culex quinquefasciatus*, is the most suspect of transmitting leprosy but is not very fit for experiments as it only bites in the dark. The use of *Stegomyia* is not advisable for various reasons. It is better to use species that bite easily when applied to the skin in tubes covered by gauze or wire-netting, such as the different species of *Mansonia*, *Tae- niphorhynchus* and *Ianthinosoma*. The easiest to procure is *Culex*, now *Ochlerotatus scapularis* which is abundant in shady gardens.

The experiments should be extensive to different species of the genus *Coccothrix* (1886), a name which has undoubted priority-rights over its synonym *Mycobacterium* (see Bibl. 4). Among these I suggest the different races of the tuberculosis bacillus and the bacillus of Stefansky, which produces a disease in rats, closely allied to leprosy.

Authentic cultures of these species can be obtained.

Various strains of bacilli isolated from leprosy should be experimented with, also, but only after the others mentioned above, especially those of tuberculosis have been tried.

In tuberculosis the more virulent strains should be excluded. The race of Guérin and Calmette may be used, but it is not favourable for experimenting with on laboratory animals. It seems more practical to work with avian or bovine tuberculosis, which lend themselves better to the purpose and are less dangerous to man. This applies also to the bacillus of Stefansky.

For infecting mosquitoes these cultures may be mixed with fresh, defibrinated, blood or diluted honey. The mosquitoes must be kept alive for some time, preferably in complete darkness, so that the experiments can be repeated and time be allowed for the incubation of the germ in the mosquito. Those which die are used for microscopical examination, after removing their legs which easily become contaminated. The proboscis must be examined separately. The salivary glands and the body can be used for inoculating into animals as well as for microscopical examination. Not only the acid-fast germs but other, similar, forms, should be looked for in both mosquitoes and inoculated animals.

The first question to solve is the length of time during which the germs may be found alive in the body of the mosquito. If they do not disappear from the internal organs at once, these may serve for inoculating into animals and for culture attempts, made at intervals.
The mosquitoes may be infected by allowing them to suck blood directly from persons or animals having the disease. This method is not very promising, unless applied to typical skin-lesions and may be used chiefly for human leprosy and Stefansky's disease in rats. If the skin is unbroken, contamination of the external parts of the mosquito can be avoided.

In the case of leprosy recent cases should be used and preferably those which are progressing, principally when there is fever, which shows that the germ is circulating in the blood.

Many years ago, I made some experiments, applying mosquitoes to leprous nodules, which are always full of acid-fast rods generally agglomerated in zoogloeae masses. I did not find acid-fast rods in the mosquitoes, but other observers seem to have met with more success. Nowadays I do not consider this negative result of much importance as I believe that though useful for diagnosis, the acid-fast forms are final and hardly infectious phases of the germ.

I would like to point out that in the hyperaemic spots, which I consider to be the first onset of the disease, acid-fast rods are mostly missing and diagnosis has to be made without their help. They may however, be found in the lymphatic glands which correspond to these initial lesions.

I consider it very important to use hyperaemic spots for infection-experiments since, in my opinion, they undoubtedly contain the virus inoculated by the mosquito-bite and are almost always found in parts of the body accessible to them, such as the face, hands and feet. They are very rebellious to local and general treatment and spread in a centrifugal direction, regardless of vascular and nervous structures.

Although as a rule tuberculosis is not transmitted by blood-sucking parasites, there is a form which is probably due to the bite of diptera. This is Lupus vulgaris also generally localised on the face and more rarely on the hands. I believe that most cases are of bovine origin, which explains the relatively mild nature of this essentially chronic disease.

There are also non-acid-fast forms of the tuberculosis germs, such as the fungoid granulations of tubercular joint-diseases.

I have often examined the urine of patients suspect of having renal tuberculosis without encountering acid-fast germs. The inoculation of small quantities of the deposit obtained by centrifugation into the groin of a guinea-pig produced swellings of the neighbouring lymphatic gland, which when extirpated, two or three weeks later, showed acid-fast bacilli.

Now as to the laboratory animals fit for these experiments: guinea-
pigs and rabbits can be used for the different forms of tuberculosis, rats for the Stefansky bacillus, monkeys for human leprosy. So as to obtain lesions, at least local ones, bites should be resorted to, either simple or repeated, or triturated mosquitoes in small doses be inoculated. They may be washed in alcohol first, or singed, so as to disinfect the outer parts. Appropriate culture-media may be inoculated in the same way.

These experiments must be repeated again and again if positive results are to be obtained. It will be enough, however, to obtain them with one of the germs used in order to demonstrate the possibility of the transmission of Coccolthrix species by mosquitoes.

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